Dockets Management Branch (HFA-305),
Food and Drug Administration,
5630 Fishers Lane (Room. 1060),
Rockville, MD 20852.
USA

26th November 2002

RE: Comments on "Draft FDA Guidance for Industry; Electronic Records; Electronic Signatures, Electronic Record maintenance" Docket No. 00D-1539

Dear Sir/Madam:

GlaxoSmithKline a research-based pharmaceutical company is engaged in the discovery, development, manufacture, and sale of pharmaceutical products. We welcome the opportunity to submit comments on aspects of the Draft Guidance.

General Comments:

1) The Draft Guidance suggests that the scope of records governed by 21 CFR Part 11 is restricted to those records identified by Predicate Rules. We suggest a supporting statement be added to clarify whether or not electronic records submitted to FDA under requirements of the Federal Food, Drug and Cosmetic Act and the Public Health Service Act, even if such records are not specifically identified in Agency regulations, are also in scope as per current 21 CFR Part 11.1(b) requirements.

2) Predicate Rules refer to broad classes of record. It is not always clear when raw data and intermediate results becomes a record and hence requires the maintenance activities set out in this Draft Guidance. It is not practical, for example, to expect the creation, maintenance, and retention of audit trail and meta-data for the huge volumes of data temporarily stored in real-time manufacturing control systems. We suggest the audit trail and meta-data controls required by 21 CFR Part 11 are inappropriate for raw data and intermediate results.

3) Many of the expectations set out in this Draft Guidance depend on the technical capability of computer applications to support 21 CFR Part 11 functionality. The Draft Guidance does not address how organizations comply when required functionality is not available in the commercial off-the-shelf products currently used to support data maintenance. To rely solely on replacing standard products with custom software developments would not seem a practical way forward. We suggest specific guidance be developed on how manual ways of working can be used to support existing technology in addressing the spirit of 21 CFR Part 11 functional requirements.

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Specific Comments:

1) Section 2 Scope. The scope does not explicitly state that the Draft Guidance covers archiving although the guidance deals with electronic record maintenance through record retention periods. We suggest this section directly refer to archiving in line with the description provided by GLP Predicate Rule [21 CFR Part 58] to avoid any potential inconsistency.

2) Section 5.1 Procedures for Electronic Records Maintenance Should Be Established And Followed. We suggest that even though record retention is outside the scope of this guidance (see section 4.2) a bullet point should be added for completeness to include procedures to ensure records are retained for their defined retention periods specified by Predicate Rules.

3) Section 5.2 Factors That Might Affect The Reliability of Electronic Records During the Required Record Retention Period Should be Identified And Controlled. We suggest changing the wording '*You should identify and control factors that...*' to '*You should identify, and as far as reasonably practical, control factors that...*' in recognition that not all risks can be completely mitigated.

4) Section 5.2 Factors That Might Affect The Reliability of Electronic Records During the Required Record Retention Period Should be Identified And Controlled. Clarification is requested as to what 'encoded' data means as we are uncertain whether any additional specific controls are being implied.

5) Section 5.2 Factors That Might Affect The Reliability of Electronic Records During the Required Record Retention Period Should be Identified And Controlled. We suggest including an additional item in the bullet point list of factors affecting record reliability to capture linked electronic signatures and audit trails.

6) Section 5.3 Continued Availability and Readability of Electronic Record Information Should Be Ensured. The current last paragraph makes reference to most important electronic records being stored separately from primary records. We suggest the final sentence giving a specific example be replaced with a general principle that appropriate controls are used to protect and secure backups and archives.

7) Section 5.3 Continued Availability and Readability Of Electronic Record Information Should Be Ensured. We suggest this section include a statement at the end of the second paragraph that the integrity of electronic records during any conversion/copying should be verified.

8) Section 5.5 The Ability To Process an Electronic Record's Information Throughout It's Record Retention Period Should Be Preserved. The requirement to reprocess records from information and meta-data would appear to be an extension to the original scope of Part 11 which requires that systems be able "to generate accurate and complete copies of records...suitable for inspection, review, and copying by the agency" [21 CFR Part 11.10(b)]. There is no equivalence here to requirements for paper-based records. We suggest it should be sufficient to provide evidence such as audit trail information that supports the integrity of a record without the need to reprocess it from scratch. If this principle was accepted it would alleviate many of the technical problems associated with long term archiving.

9) Section 6.1 The Time Capsule Approach. There is no guidance on what would constitute an acceptable way to handle electronic records that can only be maintained on their original application, when that original application is no longer supported by the vendor. We would like to reinforce the sentiment in this section that the time capsule approach is only feasible in very limited circumstances due to issues with maintaining functionality of old systems and likely withdrawal of maintenance support for legacy products from original vendors. We suggest where migration to a new electronic record keeping system is not feasible that paper copies of electronic records, checked and verified as true copies (complete with audit trails and meta-data), are deemed acceptable records for long-term retention.

10) Section 6.2 The Electronic Records Migration Approach. This section includes the statement '*However, you should carefully consider when it would be prudent to discard the old electronic records/system*'. We suggest that this statement be clarified so that the inferred time capsule approach is not required after records have been successfully migrated to a new system. The feasibility of the time capsule approach is limited (see comment 7 above).

11) Section 6.2 The Electronic Records Migration Approach. A new paragraph should be added that allows records to be retained in a format different to their creation where that removes dependency on possibly superseded technology, and the integrity of the record during any conversion/copying can be validated.

12) Section 6.2.1.3 Electronic Record Integrity Attributes Should be Preserved. This section implies that only information about creation, modification and deletion of an electronic record need be preserved. Clarification is requested regarding consistency with 21 CFR Part 11.10(e) which also requires audit trail and meta-data to be retained.

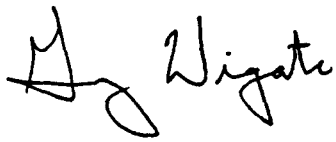
Section 6.2.1.3 Electronic Record Integrity Attributes Should be Preserved. The principle of creating new audit trail entries as records are copied during migration could set an unwarranted precedent for copy processes that operate when records are transmitted over integrated communication networks. We suggest that an audit trail entry is not required unless the content and meaning of a migrated record has been modified by operator intervention. A single audit trail entry (or similar record) at the system level designed to register the fact that a migration process has occurred should be sufficient.

13) Section 6.2.1.4 The Ability to Process Information in Electronic Record Should be Preserved. Reprocessing electronic records is an extension of the scope of Part 11 (see comment 6 above). We suggest that it should be sufficient for someone reviewing the migrated records to be able to reconstruct events to determine if the electronic record meets Predicate Rule content and signing requirements.

14) Section 6.2.1.5 Unavoidable Differences and Losses Should be Accounted For and Explained in the Migrated Electronic Record or New System Documentation. It is not clear if a third-party has to be independent to the company conducting migration, or just independent to the team conducting the migration but still within the same overall company organization. The use of the phrase 'digital signature' in this context may be better replaced with 'electronic signature' for consistency with Part 11. Migration of large volumes of data may involve many tens of thousands of individual electronic records. We question the practicality of applying a third party verification signature to each record and propose that the combination of validating the migration process and logging appropriate audit trail entries (when changes in content and meaning have occurred, see comment 13 above) should be sufficient.

We appreciate the opportunity to comment. Thank you for your consideration.

Sincerely,



Dr Guy Wingate
Director, Global Computer Validation